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Speech and language markers of neurodegeneration: a call for global equity

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In the field of neurodegeneration, speech and language assessments are useful for diagnosing aphasic syndromes and for characterizing other disorders. As a complement to classic tests, scalable and low-cost digital tools can capture relevant anomalies automatically, potentially supporting the quest for globally equitable markers of brain health. However, this promise remains unfulfilled due to limited linguistic diversity in scientific works and clinical instruments.

Here we argue for cross-linguistic research as a core strategy to counter this problem.

First, we survey the contributions of linguistic assessments in the study of primary progressive aphasia and the three most prevalent neurodegenerative disorders worldwide—Alzheimer's disease, Parkinson's disease, and behavioural variant frontotemporal dementia. Second, we address two forms of linguistic unfairness in the literature: the neglect of most of the world's 7000 languages and the preponderance of English-speaking cohorts. Third, we review studies showing that linguistic dysfunctions in a given disorder may vary depending on the patient's language and that English speakers offer a suboptimal benchmark for other language groups. Finally, we highlight different approaches, tools and initiatives for cross-linguistic research, identifying core challenges for their deployment.

Overall, we seek to inspire timely actions to counter a looming source of inequity in behavioural neurology.

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Introduction

Speech and language assessments are a pillar of neurodegeneration research. They are vital for diagnosing syndromes involving perisylvian damage, such as the non-fluent, semantic and logopenic variants of primary progressive aphasia.[1] Moreover, they are useful for characterizing, phenotyping and monitoring more prevalent conditions with distinct anatomical vulnerabilities, including Alzheimer's disease,[2,3] Parkinson's disease[4,5] and behavioural variant frontotemporal dementia.[6] Importantly, predominant speech and language deficits diverge among these disorders and correlate with their distinct atrophy patterns (Table 1). Thus, speech and language assessments can inform translational neurolinguistic models[26,27] and contribute to clinical diagnosis.[9]

Specific disturbances, such as those listed in Table 1, are common and fast in occurrence. Per current diagnostic criteria, speech and language impairments are the most salient feature in all persons with primary progressive aphasia.[1] Notably, they are also prevalent in the early stages of Alzheimer's disease, Parkinson's disease and behavioural variant frontotemporal dementia—often appearing alongside core memory, motoric and sociobehavioural symptoms, respectively.[28] Distinct deficits have been observed in Alzheimer's disease (lexico-semantic impairment,[2,29] simplified syntax,[13] altered figurative language processing[16]), Parkinson's disease (dysarthria,[30,31] difficulties with specific word patterns[4] and action concepts[4]) and behavioural variant frontotemporal dementia (picture naming deficits,[6,32] atypical speech rhythm, poor reading skills[6]). Some of these deficits may actually occur preclinically in each of these disorders.[3,33–36] Specific linguistic domains, then, emerge as important targets in early clinical testing of numerous populations.[37]

More particularly, language tests may be relevant for a pressing challenge of neurology: the quest for globally equitable markers of brain health.[38–40] Gold standard methods for detecting and monitoring neurodegenerative diseases are not equally available worldwide. For instance, CSF and imaging biomarkers have been deemed critical in a recent consensus for Alzheimer's disease diagnosis,[41,42] but they are scant, unevenly distributed and often unaffordable across developing countries,[43,44] which face the greatest burden of dementia.[45] In Latin America, for example, the number of cases is rapidly increasing but there is a lack of biospecimen and neuroimaging facilities, culturally valid tests and specialized staff.[46] Similar scenarios are found in other under-represented and underserved world regions, such as Africa and India.[43,44]

Given their non-invasive, cost-effective nature, speech and language tests could reveal widely applicable markers, especially via automated speech and language analysis (ASLA). ASLA offers objective, examiner-independent, multidimensional results via brief oral production tasks, through measures of the acoustic speech signal (e.g. speech timing, pitch variability) and/or its transcription (e.g. syntactic complexity, semantic specificity).[47,48] Across primary progressive aphasia variants, ASLA markers capture syndrome-specific patterns[49–53] that predict underlying neuropathology years before death[7] and correlate with variant-specific atrophy,[53–56] even longitudinally.[57] In Alzheimer's disease, they differentiate patients from healthy persons[13,58–62] and other patient groups,[63] predict overall cognitive status,[64] outperform certain cognitive tests in predicting dementia onset,[65] and correlate with volume of the hippocampus and other core atrophy regions.[66,67] In Parkinson's disease, ASLA features identify early-stage patients,[19,68] discriminate between cognitive phenotypes,[20,69,70] correlate with motor symptom severity[19,68] and track medication status.[71] In behavioural variant frontotemporal dementia, they capture prosodic[24] and linguistic[72] alterations as well as their worsening in the course of disease.[57] As a corollary, speech and language assessments and ASLA in particular, emerge as powerful tools in the pursuit of globally fair and scalable markers of neurodegeneration.[47,63,73,74]

Worryingly, however, this potential is undermined by widespread lack of linguistic diversity. Like other disciplines,[75] research on neurodegenerative conditions has neglected most of the world's 7000 languages.[76–79] Batteries for primary progressive aphasia diagnosis are validated for only a few linguistic communities, many of which use verbatim translations from West European languages.[80] Also, as shown by systematic reviews, speech and language studies across neurodegenerative diseases span fewer than 20 languages, most of them tested in only a handful of papers.[4,5,47,81–83] Of note, most languages in this literature are mainly spoken in high-income regions, which already concentrate ≈90% of dementia research.[84,85]

Table 1 Main neurolinguistic patterns reported in neurodegenerative disorders

Disorder	Main speech and/or language deficits	Neural correlates of main deficits	Key references
Non-fluent/agrammatic variant primary progressive aphasia	Impaired motor speech and/or agrammatism	Inferior frontal and motor regions	García *et al.*,[7] Gorno-Tempini *et al.*,[1] Montembeault *et al.*,[8] Tee and Gorno-Tempini,[9] Wilson *et al.*[10]
Semantic variant primary progressive aphasia	Multimodal semantic deficits	Anterior temporal lobe	
Logopenic variant primary progressive aphasia	Word-finding and phonological deficits	Parieto-temporal regions	
Alzheimer's disease	Lexico-semantic deficits, poor figurative language comprehension, simplified grammar	Hippocampal, temporal and temporo-parietal regions	Birba *et al.*,[11] Domoto-Reilly *et al.*,[12] Fraser *et al.*,[13] Grossman *et al.*,[14] Hirni *et al.*,[15] Rapp and Wild.[16]
Parkinson's disease	Hypokinetic dysarthria, morphosyntactic and action-verb deficits	Basal ganglia, thalamus, motor cortex, temporal lobe	Abrevaya *et al.*,[17] Alm,[18] Birba *et al.*,[4,11] Eyigoz *et al.*,[19] García *et al.*,[20] Grossman *et al.*[21]
Behavioural variant frontotemporal dementia	Deficits in naming prosody, reading and social concept processing	Fronto-insulo- temporal regions	Birba *et al.*,[11] Geraudie *et al.*,[6] Hardy *et al.*,[22] Hughes *et al.*,[23] Nevler *et al.*,[24] Saxon *et al.*[25]

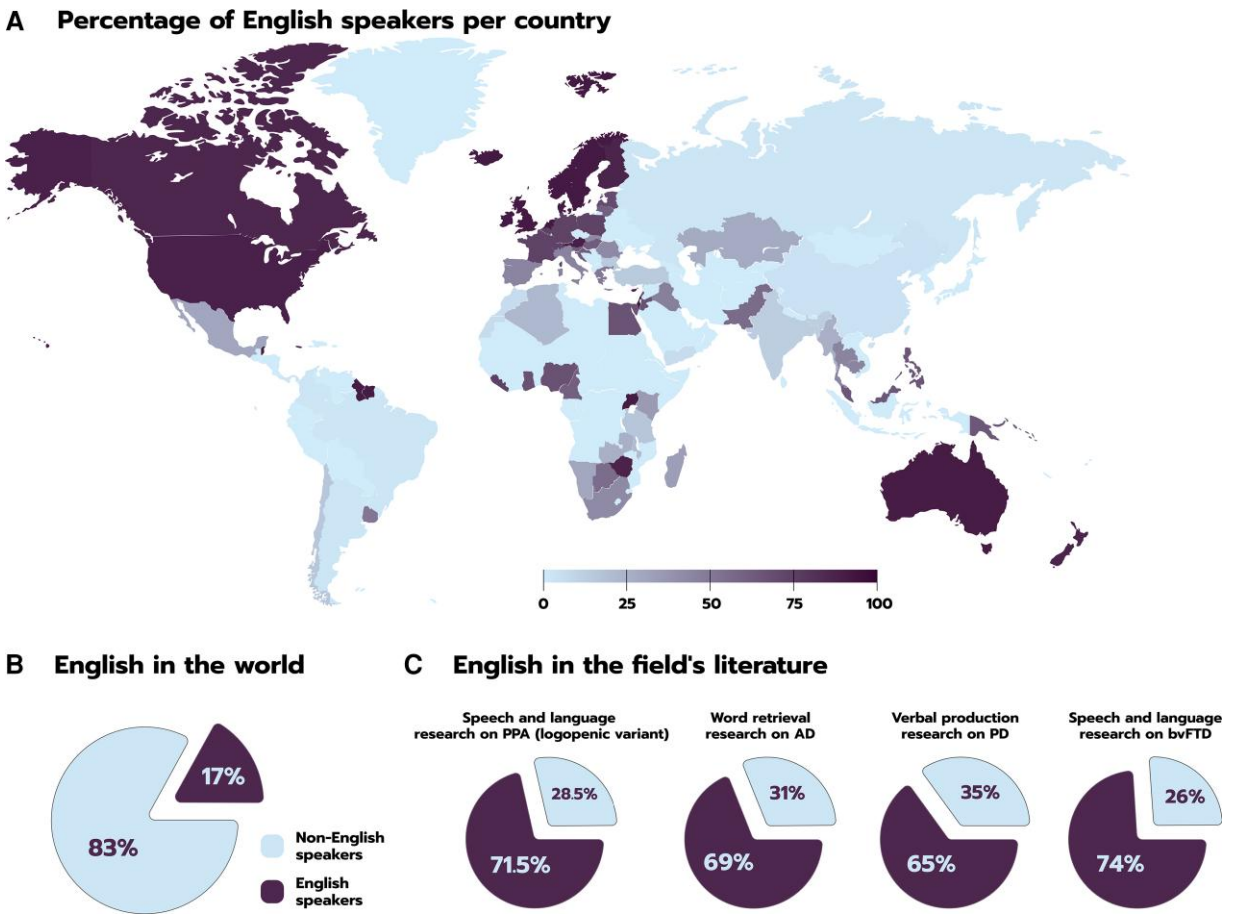

Figure 1 Anglocentrism in speech and language research on neurodegenerative disorders. (**A**) English speakers are proportionally few in most countries. (**B**) Most of the world's population speaks languages other than English. (**C**) Yet, most reports of speech and language difficulties in neurodegenerative diseases target English speakers, outnumbering studies on non-English speakers. Data were obtained from Wikipedia (https://en.wikipedia.org/wiki/List_of_countries_by_English-speaking_population) for **A**; Eberhard and Simmons[79] for **B**; and relevant reviews and/or meta-analyses for the *insets* of **C**: from *left* to *right*: Conca *et al.*,[81] Kavé and Goral,[83] Camerino *et al.*[82] and Geraudie *et al.*[6] AD = Alzheimer's disease; bvFTD = behavioural variant frontotemporal dementia; PD = Parkinson's disease; PPA = primary progressive aphasia.

Compounding these issues is the field's Anglocentrism. English is a minority language in most of the globe (Fig. 1A), being spoken to some proficiency by only 17% of the world's population (Fig. 1B).[79] Nevertheless, it dominates research on neurocognition, in general,[75] and on neurodegeneration, in particular (Fig. 1C). Diagnostic criteria for primary progressive aphasia syndromes are based on English-speaking cohorts, and tests for other populations are typically translated (though rarely adapted) from English.[80] General overviews of such syndromes exhibit the same bias. In a systematic review of logopenic variant primary progressive aphasia, for instance, 71.5% of findings came from speakers of English.[81] This language is also predominant in Alzheimer's disease research, accounting for 69% of word retrieval studies[83] and over 40% of ASLA reports[47] (with recent findings coming increasingly from the same dataset).[86] Furthermore, English has been targeted by 65% of verbal production studies on Parkinson's disease[82] and by 74% of speech and language studies on behavioural variant frontotemporal dementia[6]—few of which come from low-income (e.g. Latin American) countries.[32] Briefly, we know less about neurodegenerative disorders of language than we do about neurodegenerative disorders of one language.

Speech and language dysfunctions across languages

The above scenario would not be problematic if relations between brain and language were universal or if English were an apt model to understand every other language. *Prima facie*, this might seem the case. Typologically different languages may engage similar perisylvian regions during receptive tasks[87] and many of them share key properties with English (e.g. subject-verb agreement). Moreover, specific acoustic and discourse markers of Alzheimer's disease in English speakers may generalize onto Spanish speakers,[88] and dysarthric aspects that typify Parkinson's disease[89] and its phenotypes[20,69,90] seem similar across the languages studied so far.

Nevertheless, more fine-grained phenomena differ widely across languages and often deviate from findings in English.[75,91–93] For example, noun-verb dissociations and predominant left-hemisphere activations for pitch processing are typical in Germanic and Romance languages, but such patterns are not commonly found in Mandarin Chinese and other tonal languages.[94,95] Similarly, different fronto-posterior regions are engaged during reading depending on the script (alphabetic, in English and ideographic,

Table 2 Examples of cross-linguistic differences

Disorder	Languages	Structural contrast	Distinct marker	Key references
Non-fluent/agrammatic variant primary progressive aphasia	English	Greater phonetic and lesser morphosyntactic complexity	Phonetic distortions as most salient symptom	Canu *et al.*[98]
	Italian	Lesser phonetic and greater morphosyntactic complexity	Distinct syntactic alterations	
Semantic variant primary progressive aphasia	English	Alphabetic script (letters represent phonemes)	High prevalence of surface dysgraphia	Graham,[99] Sepelyak *et al.*,[100] Tee *et al.*[101]
	Chinese	Logographic script (logograms convey semantic or phonological information)	Low prevalence of surface dysgraphia	
Logopenic variant primary progressive aphasia	English	Less diverse morphosyntactic patterns	Frequent sentence repetition deficits	Mesulam *et al.*,[102] Hohlbaum *et al.*[103]
	German	More diverse morphosyntactic patterns	Infrequent sentence repetition deficits	
Alzheimer's disease	English	Simpler pronominal system	Overuse of pronouns	Ahmed *et al.*,[104] Fraser *et al.*,[13] Bose *et al.*[105]
	Bengali	More complex pronominal system	Underuse of pronouns	
Parkinson's disease	Spanish	Verb-framed language with rich verb vocabulary	Selective action-verb deficits	Birba *et al.*,[11] García *et al.*,[106] Møller *et al.*[107]
	Dutch	Satellite-framed language with fewer verbs	Non-selective action-verb deficits	
Behavioural variant frontotemporal dementia	No clear crosslinguistic contrast reported yet.			

in Chinese).[96] Also, while subordination (grammatical dependencies between sentence components) manifests at the syntactic level in English, it operates mainly at the morphological level in Turkish—influencing the assessment of standard tasks, such as picture description.[97] More generally, myriad phonological, orthographic, morphological, syntactic and lexico-semantic systems, as well as their interfaces with non-linguistic mechanisms, differ radically between English and most of the world's languages.[75,92] Naturally, these and other cross-linguistic differences impinge on neurolinguistic breakdown (Table 2).

As long acknowledged in stroke aphasia,[108,109] the same primary progressive aphasia syndrome may present different symptoms depending on the patient's language. For example, a picture description study on English and Italian speakers with the non-fluent/agrammatic variant revealed significantly more speech distortions in the former and distinct syntactic alterations in the latter. According to the authors, this might reflect the greater motor speech complexities of English and the elevated morphosyntactic demands of Italian's synthetic grammar (which, unlike English grammar, indicates syntactic relations through multiple word inflections for gender, person, tense and number).[98] Also, in semantic variant primary progressive aphasia, writing tests consistently reveal surface dysgraphia (spelling words via letter-sound correspondences) in English-speaking patients[99,100] but not in Chinese-speaking patients—whose writing errors, instead, abound in homophones (similar-sounding words).[101] By the same token, sentence repetition deficits in logopenic variant primary progressive aphasia may be more frequent across German speakers[103] than across English speakers,[102] arguably because German requires storing more diverse morpho-phonological patterns across stimuli. Importantly, translations of tests developed for English may overlook language-specific markers of these syndromes, compromising diagnosis.[80]

Cross-linguistic differences have also been reported in Alzheimer's disease. As shown in a machine learning study, the contribution of semantic, syntactic and paralinguistic features for disease identification differs between speakers of English and French.[110] Also, a study on error patterns[111] showed that subject omissions were recurrent in Italian-speaking patients, but absent in their English-speaking counterparts. Suggestively, note that subjects can be inferred from verbs' conjugations in Italian, but not in English (e.g. the Italian verb '*camminiamo*', on its own, entails a first person plural subject, but the English verb 'walk' can only entail first person plural if preceded by 'we'). More notably, while pronouns are often overused by Anglophone Alzheimer's disease cohorts,[13,104] their proportion is abnormally low in Bengali-speaking patients.[105] Reading dysfunctions may also depend on language (or, more particularly, on its script type), as suggested by assessments of English and Chinese-speaking persons with atypical forms of Alzheimer's disease, such as posterior cortical atrophy.[112,113] In Alzheimer's dementia, then, linguistic disruptions may be different, absent or reversed depending on the language at hand.

Linguistic idiosyncrasies are also found in Parkinson's disease research. An analysis of acoustic features[114] showed that reduced speech rhythm variability in Parkinson's disease was more marked in patients who spoke Korean than in those who spoke English, a pattern that could reflect prosodic differences—e.g. each language uses different pause and tone patterns to mark phrase boundaries, and only English uses word accents to signal new information.[115,116] Furthermore, while morphosyntactic patterns differentiated Parkinson's disease patients from healthy persons in German, Spanish and Czech, the most discriminatory features diverged across these languages (e.g. classification was mainly driven by verb-related features in Spanish and by pronoun-related features in German), arguably due to their typological grammatical differences.[19] By the same token, whereas a text comprehension paradigm revealed selective action-verb deficits in speakers of Spanish,[11,106] no such distinct impairment was observed in speakers of Danish.[107] This might be so because Spanish possesses multiple verbs that encode motion direction (resembling the English verb 'exit', which directly implies 'outwards'), while Danish features fewer, more context-sensitive verbs that require other words to encode direction (resembling the English phrase 'go out', where outwardness is conveyed by 'out').[117] In short, cross-linguistic differences also influence the utility of language markers of Parkinson's disease.

Finally, to our best knowledge, no cross-linguistic studies have been performed on behavioural variant frontotemporal dementia. Yet, some evidence suggests that lexico-semantic skills are more frequently impaired in English than in Spanish-speaking cohorts.[6] That being said, the evidence is altogether mixed,[6] calling for harmonized protocols that enable robust comparisons across languages while accounting for socio-cultural factors in this syndrome.[32]

In short, speech and language markers of neurodegeneration prove sensitive across speech communities, but they vary greatly among them. Individuals with the same diagnosis may present different verbal dysfunctions depending on their primary language and evidence from English speakers offers a suboptimal benchmark for other populations. Moreover, validated tools are unavailable for most languages and the powerful field of ASLA, based mainly on English-specific methods, is quickly reproducing these disparities. The resulting scenario is paradoxical, as potentially equitable tools seem to be generating new forms of inequity.

Ways forward and main challenges

This situation calls for a cross-linguistic and cross-cultural framework. The field requires broader representation of languages to identify their shared and distinguishing properties, leading to enhanced testing and treatment. Though still limited, existing efforts reveal fruitful ways forward.

Different approaches can be exploited to further cross-linguistic research. For example, Lindsay *et al.*[110] and Pérez-Toro *et al.*[88] performed cross-linguistic experiments by combining public data from the Pitt corpus (comprising English-speaking Alzheimer's disease patients and control subjects) with proprietary data from French and Spanish-speaking cohorts, respectively. This could be expanded onto different language pairs and replicated with public data from other conditions, including speech recordings from persons with primary progressive aphasia and Parkinson's disease in the DementiaBank. Progress can also be made through multicentric collaborations, as shown by the works of Canu *et al.*[98] on primary progressive aphasia or Eyigoz *et al.*[19] on Parkinson's disease. This can be achieved by identifying similarities among primary or secondary outcome measures in each centre's existing datasets. Even more directly, harmonized, hypothesis-driven protocols can be designed for new data collection across countries and languages.

Future efforts can benefit from existing cross-linguistic tools. For example, the Comprehensive Aphasia Test, which spans over 20 subtests of receptive and productive skills, is available in Basque, Catalan, Croatian, Cypriot Greek, English, French, Greek, Hungarian, Norwegian, Serbian, Spanish, Swedish and Turkish.[80,118] Likewise, the Quick Aphasia Battery[119] is available in English, Arabic, Danish, French, Spanish and Korean. Also, the more recent Mini Linguistic State Examination was first developed in English and has been validated in Spanish and Italian for cross-cohort comparisons.[120] Note, however, that versions of these tests vary in the parameters used for adapting the original stimuli's spelling-to-sound patterns, word properties and sentence characteristics—for details of key challenges and solutions, see Fyndanis *et al.*[118] In particular, tests may present low construct validity if based on direct translations or validated only via back-translations.[121]

Standardized tests can be complemented with experiments targeting more fine-grained hypotheses. To this end, cross-linguistically comparable stimuli can be built with multilingual resources on word frequency (e.g. Worldlex, with estimations for 66 languages derived from big data sources), phonological and lexical properties (e.g. Lexibank, offering descriptions, transcriptions and semantic glosses for over 1000 languages),[122] picture-word pairs (e.g. the MULTIMAP test, providing 218 word-image pairs matched across Spanish, Basque, Catalan, Italian, French, English, German, Mandarin Chinese and Arabic),[123] and grammar (e.g. the World Atlas of Language Structures, covering over 2600 languages).[124] Cross-linguistic resources are also available for ASLA, as seen, for example, in FreeLing, an open-source library providing diverse functionalities (e.g. part-of-speech tagging, morphological tagging, parsing, semantic role labelling) in typologically different languages (e.g. Croatian, English, Italian, Russian, Spanish, Slovene).[125] Promising avenues for cross-linguistic research also come from novel speech perception paradigms, which capture syndrome-differential deficits by manipulating temporal and spectral properties of recorded speech.[126–128] Although these resources do not cover all of the world's most spoken languages, they enable rich comparisons among patients from different speech communities.

Global language investigations can also be bolstered through formal alliances among numerous sites. ASLA research has been incorporated by the Alzheimer's Disease Neuroimaging Initiative, a long-standing multicentric effort to capture neuroanatomical, biochemical and cognitive changes in the course of Alzheimer's disease.[129] Another relevant effort can be found in the International Network for Cross-Linguistic Research on Brain Health, better known as Include (https://include-network.com/). Spanning over 60 sites in roughly 20 countries, Include fosters the discovery of language markers in under-represented languages (e.g. Hebrew, Hindi, Turkish), together with comparisons between these and more widely studied ones (e.g. English, Italian, Spanish). Collaborations are promoted among neurologists, linguists, neuroscientists, speech pathologists and engineers to jointly analyse linguistic, cognitive and imaging data via statistical and machine learning tools. New members are welcome from any world region, especially if they provide data from or access to cohorts who speak underexamined languages. With its transdisciplinary, multi-methodological ethos, Include seeks to align cross-linguistic research with current trends in behavioural and translational neurology at large.

Although extensive research of all living languages is likely unachievable, specific strategies could foster sustainable progress. For instance, primary progressive aphasia symptoms could be examined and validated in cohorts spanning diverse language families. Likewise, when investigating reading and writing deficits, users of different scripts (e.g. logographic, alphabetic, abjad abugida) should be evenly represented. Furthermore, researchers should avoid overgeneralizing their findings with universalistic claims unless adequate replications have been made on different languages. In addition, statistical harmonization methods could facilitate cross-linguistic research when tools targeting the same cognitive process in different speech communities are structured differently due to linguistic variations.[130–133] In this sense, it might be strategic to focus on under-represented languages with the largest numbers of speakers, such as those spoken in India (e.g. Hindi, Bengali, Marathi, Telugu), Indonesia (Urdu), Vietnam (Vietnamese), Africa (e.g. Swahili, Arabic, Hausa) and Latin America (Spanish, Portuguese). These efforts would be vital to bridge not only the lack of language diversity in the literature but also the need for increased neurodegeneration research in underserved regions at large.

Cross-linguistic approaches should also be pursued in the therapeutic domain. Language or typology-specific frameworks could be crucial to develop more effective treatments, beyond the importation of mainstream (often English-based) procedures. In fact,

speech assessments from trained English-speaking experts prove inaccurate when they are faced with an unknown language.[134] Rehabilitation practices might also benefit from a focus on pragmatic or broad communicative skills that may cut across language-specific differences.[135] In addition, these efforts should contemplate cross-cultural differences in attitudes towards speech disorders, which are attributed to different factors (emotional alterations, lack of effort) depending on the country.[136]

Optimal leveraging of these strategies, tools and initiatives faces numerous challenges. First, while language is widely recognized as centrally affected in primary progressive aphasia and Alzheimer's disease, it has long been described as broadly spared in Parkinson's disease and behavioural variant frontotemporal dementia.[137–139] However, recent works underscore the broad clinical utility of speech and language testing in these[4,6] and other[140] neurodegenerative disorders, even if many deficits are secondary to broader motoric or cognitive dysfunction. Wider recognition of language changes across diagnoses would be critical for cross-linguistic findings to be incorporated in clinical toolkits. Second, typological and neurocognitive differences among languages can be easily confounded with broader cultural idiosyncrasies across cohorts. New cross-linguistic studies would benefit from incorporating relevant cross-cultural measures (e.g. surveys on social determinants of health) to disentangle linguistic and non-linguistic sources of commonality and differentiation across language groups.[75] Third, financial resources are unevenly available for language research across world regions. Trans-regional funding schemes should be systematically pursued to boost research on sub-represented languages and align it with world-leading initiatives. Current and future efforts in these directions will be critical to the success of the cross-linguistic framework advocated here.

Conclusion

Speech and language assessments can reveal cognitive markers of several brain disorders in an equitable fashion. However, a global approach is necessary for these tools to be useful across languages and cultures. Incipient evidence indicates that the linguistic symptomatology of a given disease may manifest differently depending on the patients' language, calling for wider empirical diversity and comparative efforts. Increased awareness of the transdiagnostic utility of speech and language measures, their limited availability across the world's languages, and existing resources to counter this imbalance are critical to prevent the emergence of a new source of global inequity in behavioural neurology.

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Competing interests

The authors report no competing interests.

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